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**VIA CM/ECF**

The Honorable Richard G. Andrews  
United States District Court  
for the District of Delaware  
844 North King Street  
Wilmington, DE 19801

Re: *San Rocco Therapeutics, LLC v. bluebird bio, Inc., et al.*,  
C.A. No. 21-1478-RGA

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Dear Judge Andrews:

Plaintiff San Rocco Therapeutics, LLC (“SRT”) respectfully submits this explanation of the basic and novel properties of the invention in all asserted claims and proposed jury instruction in reference to the disputed term “consists essentially of.” *See* D.I. 149. As explained below, the basic and novel properties are a 3.2-kb upper limit of Locus Control Region (“LCR”) material (a type of genetic material found in human DNA). In other words, 3.2-kb serves as an upper limit on the amount of LCR material that may be included in the asserted claims.

The phrase “basic and novel properties” is used in both proposed constructions of “consists essentially of.” “A ‘consisting essentially of’ claim occupies a middle ground between closed claims that are written in a ‘consisting of’ format and fully open claims that are drafted in a ‘comprising’ format.” *PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1354 (Fed. Cir. 1998). The plain meaning is “necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention.” *See Ecolab, Inc. v. FMC Corp.*, 569 F.3d 1335, 1342-44 (Fed. Cir. 2009). The basic and novel properties are identified by looking to the intrinsic record. *See* Ex. A, *L’Oreal S.A. v. Johnson & Johnson Consumer Cos., Inc.*, C.A. No. 12-98-GMS, D.I. 196 at 2 n.2 (D. Del. Nov. 5, 2014).

For background, human DNA has globin genes (defining the makeup of globin molecules) and an LCR (for controlling those globin genes). *See* D.I. 141 at § II.A. The inventors developed a gene therapy combining a globin gene with genetic material (*i.e.* nucleotides) drawn from three regions of the human LCR. *See id.* Thus, the issued claims all recite, *inter alia*, “a 3.2-kb nucleotide fragment which consists essentially of” three fragments obtainable from the human LCR. D.I. 142-143 (“JA”) at JA0013-14 at Claims 1, 23 and JA0030-31 at Claims 1, 11. The genetic material which must be included in the 3.2-kb nucleotide fragment is from three LCR fragments that are identified by restriction site (*e.g.*, BstXI and SnaBI) locations in the LCR (*e.g.*, “a BstXI and SnaBI HS2-spanning nucleotide fragment of said LCR”). *Id.* However, the genetic material from the three LCR fragments need not “extend between” the restriction sites (*e.g.*, not all of the nucleotides between BstXI and SnaBI need to be included). *See* D.I. 141 at §§V.A.1, V.A.3, V.B.1, V.B.3. Furthermore, non-LCR material may be included in the 3.2-kb nucleotide

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fragment. *See, e.g.*, JA0009 (“the [LCR] has two introduced GATA-1 binding sites... between HS3 and HS4.... [The TNS9 embodiment has] the LCR elements, the 2 additional GATA....”).

Accordingly, the 3.2-kb nucleotide fragment must contain genetic material from the three identified LCR fragments and is open to additions. This can be more LCR material (*e.g.* using all of the LCR material “extending between” the restriction sites) or non-LCR material (*e.g.* GATA-1 binding sites). While the 3.2-kb nucleotide fragment can be made of such a mix of LCR and non-LCR material, 3.2-kb serves as an upper limit on the amount of LCR material which can be included.

During prosecution, the applicants distinguished prior art 30-kb, 22-kb, and 5.5-kb LCR fragments using 3.2-kb as an upper limit for LCR material. JA0380. The applicants stated that “[t]he relevant basic and novel properties of the claimed 3.2-kb nucleotide fragment are defined in Claim 1.” JA0379. Then-pending Claim 1 recited: “a 3.2-kb nucleotide fragment which consists essentially of.” JA0373. The applicants explained that “any additional nucleotides added to the 3.2 kb fragment that cause the fragment to exceed 3.2 kb, would alter a basic and novel property of the invention.” *Id.* JA0379-80. This makes sense: the applicants took a targeted approach as to what LCR material to include rather than a kitchen-sink approach of massive LCR fragments (*e.g.* 30-kb) or the entire human LCR which happened to contain the three required LCR fragments.

It is important to distinguish applicants’ basic and novel properties argument for an upper limit of 3.2-kb versus “extending between” in JA0377-81. In addition to the upper limit argument, applicants further distinguished the prior art using the “extending between” requirement. *See* JA0377-81 (*e.g.*, referring to the “restriction sites defining the ends of each fragment” and “size of each fragment”). However, applicants deleted the “extending between” requirement prior to issuance. JA0404-06. Thus, the applicants’ statements cannot be taken *en masse* from JA0377-81; under the *issued* claims, the three fragments are no longer limited to those “extending between” the restriction sites. D.I. 141 at §§V.A.1, V.A.3. However, under both the old claims (requiring “extending between”) and the issued claims (not requiring “extending between”), 3.2-kb is an upper limit on the total amount of LCR material. That upper limit was not changed by the deletion of “extending between.” Thus, the relevant basic and novel properties reflected in the *issued* claims is a 3.2-kb upper limit of LCR material.

SRT’s position is “consists essentially of” requires no construction. D.I. 141 at § V.A.I. Should the Court construe “consists essentially of,” the jury should be instructed as follows:

The phrase “consists essentially of” means “necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention.” Here, the basic and novel properties are a 3.2-kb upper limit of Locus Control Region (also called “LCR”) material. Thus, “consists essentially of” is open to additions not listed in the claims, provided that those additions do not result in more than a total of 3.2-kb Locus Control Region material. In other words, 3.2-kb serves as an upper limit on the amount of LCR material that may be included in the asserted claims.

Respectfully,

*/s/ Anne Shea Gaza*

Anne Shea Gaza (No. 4093)

Enclosure (Exhibit A)

cc: All Counsel of Record (via electronic mail)